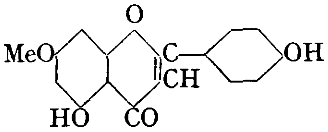
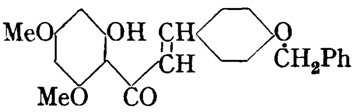
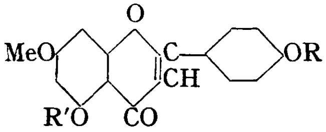
124. *Synthetical Experiments in the Chromone Group. Part XIX. A Synthesis of Genkwanin.*

By HARBHAJAN S. MAHAL and KRISHNASAMI VENKATARAMAN.

NAKAO and TSENG (*J. Pharm. Soc. Japan*, 1932, No. 602, 343; 1933, No. 608, 905) isolated genkwanin from the Chinese drug " yuen-hua " and proposed the structure (I) for it: this was confirmed by Tseng (*ibid.*, 1935, No. 636, 30) by its synthesis from phloracetophenone and *p*-benzyloxybenzoic anhydride, followed by partial methylation and debenzylation. We have synthesised genkwanin as follows: 2-*Hydroxy*-4'-*benzyloxy*-4 : 6-*dimethoxychalkone* (II) was oxidised by means of selenium dioxide (Mahal, Rai, and Venkataraman, J., 1935, 866) to the *flavone* (III; R = CH_2Ph, R' = Me); debenzylation with hydrochloric acid in acetic acid gave *genkwanin* 5-*methyl* ether (III; R = H, R' = Me), which was converted into genkwanin (I) by partial demethylation with aluminium chloride (Gulati and Venkataraman, this vol., p. 267).


(I.)


(II.)


(III.)

Although ω-benzoyl-2 : 4 : 6-trimethoxyacetophenone could be demethylated in the 2-position and cyclised to chrysin dimethyl ether in one operation by treatment with aluminium chloride in nitrobenzene, a similar reaction with the 4'-*benzyloxy*-analogue gave 5 : 7-dimethoxy-4'-benzyloxyflavone in very poor yield.

Interaction of alcoholic potash and the dibromide of the *O*-acetyl derivative of the chalkone (II) produced the corresponding coumaranone, as indicated by the colour reactions, and not the flavone (III).

EXPERIMENTAL.

ω-4'-*Benzyloxybenzoyl*-2 : 4 : 6-*trimethoxyacetophenone*.—A mixture of 2 : 4 : 6-trimethoxyacetophenone (3 g.), methyl *p*-benzyloxybenzoate (7·2 g.), and sodium dust (0·5 g.) was heated at 120° for 3 hours. After treatment with ice-water the liquid was filtered and saturated with carbon dioxide. The precipitated *diketone* crystallised from alcohol in yellow needles (1·1 g.), m. p. 101—102°, which gave a dark red colour with alcoholic ferric chloride (Found *: C, 71·5; H, 5·8. $C_{25}H_{24}O_6$ requires C, 71·4; H, 5·7%).

2-*Hydroxy*-4'-*benzyloxy*-4 : 6-*dimethoxychalkone* (II).—2-Hydroxy-4 : 6-dimethoxyacetophenone (Gulati and Venkataraman, *loc. cit.*, 7 g.) and *p*-benzyloxybenzaldehyde (9 g.), by treatment with alcoholic caustic soda, gave the *chalkone*, which crystallised from glacial acetic acid in golden-yellow needles (7 g.), m. p. 159° (Found: C, 73·6; H, 5·7. $C_{24}H_{22}O_5$ requires C, 73·8; H, 5·6%), and developed a deep red colour with alcoholic ferric chloride. The *acetyl* derivative, stout colourless needles from alcohol, melted at 105° (Found: C, 72·0; H, 5·7. $C_{26}H_{24}O_6$ requires C, 72·2; H, 5·6%).

4'-*Benzyloxy*-5 : 7-*dimethoxyflavone* (III; $R = CH_2Ph$, $R' = Me$).—A mixture of (II) (7 g.), selenium dioxide (7 g.), and amyl alcohol (100 c.c.) was refluxed for 12 hours, the selenium removed and washed with ether, and the combined solutions extracted with 20% aqueous caustic soda; the precipitated solid was collected (3·5 g.), and removal of the solvents from the ether–amyl alcohol layer by warming on the water-bath, followed by steam distillation, gave more (1·5 g.) of the same substance. Two crystallisations of the combined product from alcohol gave orange-yellow needles, m. p. 178°, exhibiting no ferric chloride reaction (Found: C, 74·3; H, 5·4. $C_{24}H_{20}O_5$ requires C, 74·2; H, 5·1%).

Genkwanin 5-*Methyl Ether* (III; $R = H$, $R' = Me$).—The debenzylated substance obtained from 3·5 g. of the benzyl ether crystallised from alcohol in pale yellow needles (1·6 g.), m. p. 298° (Found *: C, 68·2; H, 4·9. $C_{17}H_{14}O_5$ requires C, 68·4; H, 4·7%), which gave a pale brown ferric chloride coloration. The *acetyl* derivative crystallised from alcohol in colourless needles, m. p. 220° (Found *: C, 66·6; H, 4·5. $C_{19}H_{16}O_6$ requires C, 67·0; H, 4·7%).

Genkwanin (I).—The above methyl ether (0·5 g.), aluminium chloride (0·6 g.), and nitrobenzene (3 c.c.) were heated on a boiling water-bath for 1 hour, ice and hydrochloric acid added, the nitrobenzene removed with steam, and the residue acetylated by means of acetic anhydride and pyridine. The fine colourless needles (0·2 g., from alcohol) of the acetate had m. p. 197—198°, undepressed by the acetate of natural genkwanin (Found *: C, 64·9; H, 4·2. Calc. for $C_{20}H_{16}O_7$: C, 65·2; H, 4·3%). Hydrolysis of the acetate, by warming with 50% hydrochloric acid on the water-bath for a few minutes, and crystallisation from aqueous acetone gave bright yellow needles, m. p. and mixed m. p. with natural genkwanin, 285—286° (Found *: C, 67·9; H, 4·6. Calc. for $C_{16}H_{12}O_5$: C, 67·6; H, 4·2%). The colour reactions also were identical.

The analyses marked * were carried out by Dr. Ing. A. Schoeller. We are grateful to Principal T. S. Wheeler of the Royal Institute of Science for facilities in his laboratory afforded to one of us (H. S. M.), who wishes also to thank the Lady Tata Memorial Trust for a scholarship. We are deeply indebted to Dr. Kwong-fong Tseng for specimens of genkwanin and diacetylgenkwanin.

ROYAL INSTITUTE OF SCIENCE, BOMBAY.
THE UNIVERSITY, BOMBAY.

[*Received, January 20th*, 1936.]